REMARKS

I. An IDS is submitted herewith.

II. The claim objections and 112 issues have been respectfully addressed.

Applicants respectfully thank the Examiner for detailing the points at pages 2-4 of the Office Action which all have respectfully been addressed herein. These amendments were made for matters of form such as antecedent basis. Therefore, these amendments were respectfully made merely for reasons tangential to any equivalents. No new matter has been added.

III. The anticipation rejections of claims 1-3, 7, 10, 14, 20, 21, 24, 25, 26, 32, 42, 43, 45, 48, 52, 55, 62, 63, 66, 67, 68, 74, 83, and 84 under 35 U.S.C. 102(b) by Yang (U.S. 5,859,700).

Claims 1 and 48 are the independent claims. Claim 1 claims:

1. (Amended) A method for optical detection of characteristic quantities of the wavelength-dependent behavior of an illuminated specimen in an image generating arrangement, such as the emission behavior, [and/or] absorption behavior, [preferably the] fluorescence, [and/or] luminescence, [and/or] phosphorescence, [and/or] enzyme-active light emission, [and/or] or enzyme-active fluorescence of the illuminated specimen, comprising:

determining at least one spectral centroid [and/or] and;

determining a maximum of [the] emission radiation and/or of [the] absorbed radiation of the illuminated specimen.

Claim 48 claims:

48. (Amended) An arrangement for optical detection of characteristic quantities of the wavelength-dependent behavior of an illuminated specimen, particularly the emission behavior, [and/or] absorption behavior, [preferably the] fluorescence, [and/or] luminescence, [and/or] phosphorescence, [and/or] enzyme-active light emission, [and/or] or enzyme-active fluorescence of an illuminated specimen, comprising:

means for determining at least one spectral centroid, [and/or]

and means for determining a maximum of [the] emission radiation, [and/or] or of [the] absorbed radiation.

In regard to Yang.

Yang U.S. 5,859,700 describes special arrangements and methods for displaying spectra and for extracting determined properties.

However, ***in Yang, there is no determination of the spectral centroid***; rather, there is only a simultaneous recording of spectra or different specimen points (col. 3, lines 30-35). A **centroid** is commonly defined as "the point at the center, the sum of the displacements of all points in the figure."

In the present invention, as claimed in claims 1 and 48 **a determination step (or means for) of the spectral centroid of an illuminated specimen,** (for example one with naturally occurring dyes in a living tissue specimen) is used to create the position signal which is a measure of the position of the centroid of the emission spectrum. (see page 12, lines 20-21).

Thus is it very significant that, **the determination, *per se* of the spectral centroid is not disclosed by Yang**, i.e., as described on page 11 of the present specification:

> "As will be seen from Figs. 3 and 4, the individual dyes differ with respect to the position and shape of the emission spectra. **The algorithm (Fig. 7) determines, per image point, the position of the centroid** and maxima of the emission signal detected in the image point..."

Thereafter, "Different dyes can be distinguished based on their position and type of emission spectra by measuring the position signal." (see page 12, lines 3-6) Also, as described at page 13

> "The decisive advantage of the method consists in that the fluorescence of each dye in its entirety (sum signal) can be detected independent from the degree of overlap of the emission spectra and, nevertheless, the dyes can be shown separately **(by the position signal).** Heavily overlapped dyes (Fig. 3c) can therefore be detected particularly efficiently."

None of the above is taught or enabled by Yang, because the claimed limitations of :

"determining at least one spectral centroid" claim 1, and

"means for determining at least one spectral centroid" of claim 48,

are not taught by Yang for anticipation purposes. Applicants also note that these limitations are not suggested by Yang for obviousness purposes. Therefore, as the remaining claims depend from claims 1 and 48, they are also respectfully asserted to be allowable.

<u>Applicants note other points regarding Yang</u>

Applicants note the following points as they may affect the claims and the motivation of one skilled in the art to combine Yang with another reference.

1. Yang is not confocal (col. 3, lines 30-35 and claim 1).

2. Yang does not use any dispersive elements for the simultaneous recording of the spectral information on a matrix detector. Rather, the entire specimen is observed in widefield and the wavelength of the narrow-band light source is varied for recording the absorption spectrum.

3. The extraction of features (edge detection) relates to the spatial structure and is carried out by means of summing the grayscale values of a pixel surface of 3x3 pixels. Subsequently, it is checked whether or not the sum of a determined inequality is sufficient. Depending on the match, a corresponding grayscale value is assigned to the pixel (see Fig. 1). This extraction is not based on a calculation of spectral values and is accordingly not suitable for separate display of dye signatures since there is no weighting of the spectral components.

4. In addition, the shown arrangement is not suitable for confocal microscopy.

<u>IV. The obviousness rejections of dependent claims 4-6, 8, 9, 13, 15, 17-19, 49-51, 53, 54, and 58-61 under 35 U.S.C. 103(a) over Yang (U.S. 5,859,700) in view of Okubo (EP 0463 600A).</u>

The Office Action states that Yang lacks the teaching of weighting of signals from individual channels through the use of weight curves. Therefore, the USPTO cites Okubo for teaching the use of weight curves, and states that it would have been obvious to use a weighting curve to analyze the data collected by Yang for the more precise and reliable calculations.

a) Object and field of application are in both Yang and Okubo are different - spectroscopy vs. fluorescence microscope (image-generating).

b) In Okubo, calibration of center wavelengths is carried out by oversampling of the spectrum of a narrow-band light source beyond the spectral resolution (HWB) of the

spectrometer. In the presently claimed invention, a high optical-spectral resolution (HWB) of about 1 nm, but with a low sampling resolution of approximately 10 nm is used, so that only a few data points need to be evaluated for identification of spectrally broadband dyes with a weighting algorithm (centroid determination). Therefore, citing Okubo in combination with Yang (see 1.) does not each or suggest all of the limitations of the claims.

<u>V. The obviousness rejections of claims 11, 12, 27, 56, 57, and 69 under 35 U.S.C. 103(a) over Yang (U.S. 5,859,700) in view of Lee (U.S. 5,737,077).</u>

The USPTO incorrectly equates the function of resistor R1 in Lee with the function of the present invention's claimed resistor cascade or chain for determining the centroid. The function of R1 in Lee is described in col. 10, lines 25, 28 and 33, 34. It is used to adjust the gain of the transimpedance amplifier. In present invention as claimed, the resistors are used to determine the centroid (position signal) and sum signal. Therefore, they limitations are not taught or suggested by Lee.

<u>VI. The obviousness rejections of claims 22, 23, 64 and 65 under 35 U.S.C. 103(a) over Yang (U.S. 5,859,700) in view of Okubo (EP 0463 600A) as applied to claims 8 and 53 above, and further in view of Hochman (U.S. 6,319,682).</u>

Hochman US 6,319,682 ,Col. 12, lines 12 - 15, describes a look up table for the values of the signals, i.e., it mirrors the spatial structure. This shows the prior art. In the present invention as claimed, however, the look up table is determined by the position of the spectral centroid. Therefore, this look up table is fundamentally different than that described in than what is taught or suggested by Hochman.

<u>VII. The obviousness rejections of claims 28-30, 34, 70-72, and 76 under 35 U.S.C. 103(a) over Yang (U.S. 5,859,700) in view of Kash (U.S. 6,342,701).</u>

Kash US 6342701 describes a device for time-correlated single-photon counting (abstract). Photon counting is indeed known and prior art. However, a spectrally resolved

photon counting with subsequent determination of the centroid is carried out in claimed present invention. This is not mentioned in Kash.

VIII. The obviousness rejections of claims 35, 39, 41, 44, 46, 77, 81, 82, 85, and 86 under 35 U.S.C. 103(a) over Yang (U.S. 5,859,700) in view of Simon (U.S. 6,356,088) or Yagi (U.S. 5,986,256). or Tuuannen (U.S. 6,084,680).

Applicants respectfully assert that due to the deficiencies in the Yang refernces as discussed above at III., the cited references do not make up for those deficiencies in combination and therefore, these dependent claims should also be allowable.

IX. Conclusion.

In light of the *FESTO* case, no claim amendment or argument made herein was related to the statutory requirements of patentability unless expressly stated herein. No claim amendment or argument made was for the purpose of narrowing the scope of any claim unless Applicant has explicitly stated that the argument is "narrowing." Thus, the amendments herein were made for no more than a "tangential relation" for any equivalents unless explicitly stated that they were not a "tangential relation" reason for amendment or argument. Therefore, it is respectfully requested that all of the claims be reconsidered and allowed.

Please call the undersigned for any reason to expedite prosecution of this application.

Respectfully submitted,

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MARKED-UP CLAIMS

Please amend claims as follows:

1. (Amended) A method for optical detection of characteristic quantities of the wavelength-dependent behavior of an illuminated specimen in an image generating arrangement, such as the emission behavior, [and/or] absorption behavior, [preferably the] fluorescence, [and/or] luminescence, [and/or] phosphorescence, [and/or] enzyme-active light emission, [and/or] or enzyme-active fluorescence of the illuminated specimen, comprising:

determining at least one spectral centroid [and/or] and;

determining a maximum of [the] emission radiation and/or of [the] absorbed radiation of the illuminated specimen.

2. (Amended) The method according to claim 1, wherein the determination of the centroid [and/or] and of the maximum of the emission radiation of fluorochromes is carried out for distinguishing different dyes [and/or] or for determining the local dye composition of an image point when a plurality of dyes are used simultaneously [and/or] or for determining the local shift of the emission spectrum depending on the local environment to which the dye or dyes is or are attached [and/or] or for measuring emission ratio dyes for determining ion concentrations.

3. (Amended) The method according to claim 1, wherein the determination of the centroid [and/or] and of the maximum of the reflected or transmitted excitation radiation of fluorochromes is carried out for distinguishing different dyes [and/or] or for determining the local dye composition of an image point when a plurality of dyes are used simultaneously [and/or] or for determining the local shift in the absorption spectrum depending on the local environment to which the dye or dyes is or are attached [and/or] or for measuring the absorption ratio for determining ion concentrations.

4. (Amended) The method according to claim 1, further comprising splitting [wherein] the emission radiation of the specimen [is split by] a dispersive element and is detected in a spatially resolved manner in at least one direction.

5. (Amended) The method according to claim 1, further comprising splitting [wherein a splitting of] the fluorescent radiation [is carried out].

6. (Amended) The method according to claim 1, further comprising splitting [wherein] the radiation reflected or transmitted by the specimen is split by a dispersive element for absorption measurement and is detected in a spatially resolved manner in at least one direction.

7. (Amended) The method according to claim 1, further comprising carrying out [wherein] a spectral weighting [is carried out] between a plurality of detection channels,

summing of [the] weighted channels of [the] signals of the detection channels; and

summing of the detection channels is carried out.

8. (Amended) The method according to claim 1, further comprising weighting [wherein] the signals of the detection channels [are weighted] in that they are multiplied by a weighting curve,

generating a sum signal [is generated] in that the sum of the channels taken into account is determined, and

generating a position signal is generated in that the sum of [the] weighted signals is divided by the sum signal.

10. (Amended) The method according to claim 1, further comprising:

[wherein] converting signals of detection channels [are converted and digitally] digitally;

[read] reading out the signals of the detection channels and;

[the] weighting and summing the signals of the detection channels [are carried out] digitally in a computer.

11. (Amended) The method according to claim 10, wherein the weighting and summing of the signals of the detection channels are carried out with analog data processing by means of a resistance cascade.

12. (Amended) The method according to claim 11, [wherein the] further comprising adjusting the resistances [are adjustable].

13. (Amended) The method according to claim 8, [wherein the] further comprising adjusting the weighting curve [is adjustable].

14. (Amended) The method according to claim 1, [wherein the] further comprising influencing the signals of detector channels [are influenced] by a nonlinear distortion of the input signals.

15. (Amended) The method according to claim 1, [wherein] further comprising adjusting the integration parameters [are influenced].

16. (Amended) The method according to claim 1, [wherein the] further comprising adjusting a characteristic or response curve of an amplifier [is influenced].

17. (Amended) The method according to claim 8, [wherein the] further comprising determining in analog a position signal and;

determining in analog the sum signal [are determined in analog, converted],

converting the position signal and the sum signal and;

[read] reading out digitally the position signal and the sum signal.

18. (Amended) The method according to claim 7, wherein an upper and a lower signal corresponding to the sum of the signals of [the] individual channels which are weighted by opposing weighting curves are read out, digitally converted and fed to the computer.

19. (Amended) The method according to claim 8, wherein [the] a position signal and the sum signal are used to generate an image.

22. (Amended) The method according to claim 8, wherein [the] a position signal and the sum signal are combined with a lookup table.

24. (Amended) The method according to claim 1, wherein a comparison of a measured signal with a reference signal is carried out via comparators in detection channels and in case the

reference signal is not reached [and/or] or is exceeded a change in [the] a operating mode of [the] a detection channel is carried out.

25. (Amended) The method according to claim 24, wherein [the] a respective detection channel is switched off [and/or] or not taken into account.

26. (Amended) The method according to claim 1, wherein [the] a relevant spectral region is narrowed in this way.

27. (Amended) The method according to claim 1, wherein [the] signals of detection channels are generated by at least one integrator circuit.

28. (Amended) The method according to claim 1, wherein [the] signals of detection channels are generated by photon counting and subsequent digital-to-analog conversion.

29. (Amended) The method according to claim 1, wherein [the] a photon counting is carried out in time correlation.

37. (Amended) The method according to claim 1, using an X-Y scanner in [the] illumination means.

48. (Amended) An arrangement for optical detection of characteristic quantities of the wavelength-dependent behavior of an illuminated specimen, particularly the emission behavior, [and/or] absorption behavior, [preferably the] fluorescence, [and/or] luminescence, [and/or] phosphorescence, [and/or] enzyme-active light emission, [and/or] or enzyme-active fluorescence of an illuminated specimen, comprising:

means for determining at least one spectral centroid, [and/or]

and means for determining a maximum of [the] emission radiation, [and/or] or of [the] absorbed radiation.

52. (Amended) The arrangement according to claim 48, wherein a spectral weighting is carried out between a plurality of detection channels, summing of [the] weighted channels of the

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signals of the detection channels and summing of [the] detection channels is carried out.

53. (Amended) The arrangement according to claim 52, wherein [the] signals of detection channels are weighted in that they are multiplied by a weighting curve, a sum signal is generated in that the sum of the channels taken into account is determined, and a position signal is generated in that the sum of [the] weighted signals is divided by the sum signal.

55. (Amended) The arrangement according to claim 52, wherein signals of detection channels are converted and digitally read out and [the] weighting and summing are carried out digitally in a computer.

57. (Amended) The arrangement according to claim 56, wherein [the] resistances are adjustable.

59. (Amended) The arrangement according to claim 53, wherein [the] <u>a</u> position signal and the sum signal are determined in analog, converted, and read out digitally.

60. (Amended) The arrangement according to claim 52, wherein an upper and a lower signal corresponding to the sum of the signals of [the] individual channels which are weighted by opposing weighting curves are read out, digitally converted and fed to the computer.

61. (Amended) The arrangement according to claim 53, wherein [the] <u>a</u> position signal and the sum signal are used to generate an image.

64. (Amended) The arrangement according to claim 53, wherein [the] <u>a</u> position signal and the sum signal are combined with a lookup table.

66. (Amended) The arrangement according to claim 48, wherein a comparison of a measured signal with a reference signal is carried out via comparators in detection channels and in case the reference signal is not reached [and/or] <u>or</u> is exceeded a change in [the] <u>a</u> operating mode of [the] <u>a</u> detection channel is carried out.

67. (Amended) The arrangement according to claim 48, wherein [the] a respective detection channel is switched off and/or not taken into account.

68. (Amended) The arrangement according to claim 48, wherein [the] a relevant spectral region is narrowed in this way.

71. (Amended) The arrangement according to claim 70, wherein [the] a photon counting is carried out in time correlation.

79. (Amended) The arrangement according to claim 48, including an X-Y scanner in [the] illumination source.